

REMARKS

Claims 1-11, 16, 17 and 19 are pending, claim 21 is new and claims 1 and 16 are amended. Claim 21 includes subject matter of claim 19 and claim 16 is amended to clarify the extracellular matrix from a cell retrieved from a subject is placed into a tissue subjacent to the vocal cord defect in the same subject. No prohibited new matter is added upon entry of new claim 21 or amended claim 16. In the Office action, the claims were rejected over Naughton (U.S. Pub. No. 2002/0038152 A1), Boss Jr. (U.S. Patent No. 5,591,444) and Daniels *et al.* (U.S. Patent No. 3,949,073). The rejections are traversed for the reasons set forth below.

Rejection of the Claims under 35 U.S.C. § 102

Claims 1-8, 11, 16 and 17 were rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Naughton. The rejection is respectfully traversed. Naughton discusses corrective processes in which an extracellular matrix is generated from cells *in vitro*, the cells are destroyed, and the extracellular matrix is separated from other tissue culture components before it is injected into the subject's skin. Specifically, Naughton kills the cells by such methods as flash-freezing the cells without a cryopreservative and irrigating the cells with a hypotonic solution such as sterile water (see paragraph 6.7 of the document). Also, Naughton characterizes the extracellular matrix as a framework of proteins (*e.g.*, collagens, growth factors, and adhesion molecules), not cells (see paragraph 34). Thus, the step of separating the dead cells from the extracellular matrix yields a product free of cells, and even if a few cells are not separated from the extracellular matrix, these cells are dead and not viable as a result of the step of killing the cells. Further, the cells from which the extracellular matrix is separated are not specifically from the subject to whom the extracellular matrix is delivered. Due to these features of the Naughton process, there are at least four reasons why Naughton fails to anticipate the methods of claims 1-11, 16, 17 and 19 in the subject patent application.

First, claims 1-11 and 19 are directed to methods for correcting a vocal cord defect in which viable cells from the subject are cultured *in vitro* and these cells then are introduced to the subject in a position subjacent to the vocal cord defect. Naughton fails to disclose methods in which cells are delivered to a position subjacent to a vocal cord defect, because the process disclosed in

that document separates any cells from the extracellular matrix before the cell-free extracellular matrix is injected into the subject's skin. Claims 1-11 and 19 therefore are not anticipated by Naughton because they specify that cells, not a separated cell-free extracellular matrix, are delivered to a position subjacent to the vocal cord defect. / NO

Second, claims 1-11 and 19 specify that viable cells are placed in a position subjacent to the vocal cord defect. Because Naughton first destroys the cells before the extracellular matrix is separated from the cells and the supporting medium, the cited document fails to disclose methods in which viable cells are placed in a position subjacent to a vocal cord defect. Thus, Naughton cannot anticipate claims 1-11 and 19. / yes he does

Third, claims 1-11 and 19 specify that viable cells from a subject are placed into a tissue of the same subject. While Naughton discusses methods in which cells are derived from biopsies, cadavers and foreskin (*see e.g.* paragraph 0048), the document does not specifically disclose methods in which cells derived from a subject are delivered to the same subject after manipulation.

Fourth, Naughton fails to anticipate claim 19 as the document does not disclose methods of delivering a viable cell to the specific regions referenced in the claim, and therefore the Office correctly did not reject claim 19 over Naughton. / not claimed

Claims 16, 17 and 21 also are not anticipated by Naughton. Amended claim 16 specifies that the extracellular matrix from cells retrieved from a subject are placed into a tissue subjacent to the vocal cord defect in the same subject. As described in the previous paragraphs, Naughton does not specifically disclose methods in which material derived from a subject is placed into a tissue of the same subject. And Naughton does not disclose methods for introducing an extracellular matrix to the tissues specified in claim 21. Thus claims 16, 17 and 21 are not anticipated by Naughton. / yes he does

Accordingly, it is respectfully requested that the Office withdraw the rejection of the claims under 35 U.S.C. § 102.

Rejection of Claims Over Boss and Daniels

Claims 1-4, 6-11, 16, 17 and 19 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Boss in view of Daniels. The Office based the rejection on an interpretation of Boss disclosing autologous cell corrective surgery for improving depressed scars and wrinkles in the skin but not vocal cord defects. The Office combined Boss with Daniels, and interpreted the latter

as teaching a method for corrective surgery of depressed scars, wrinkles and vocal cord defects. The Office also stated that Daniels disclosed a process of washing with a phosphate buffered saline solution and the use of collagen to cause rapid colonization after implantation. The applicants respectfully traverse this rejection.

Boss discusses methods for repairing facial tissue in a subject, such as laugh lines, perioral wrinkles, galbellar furrows, depressed scars, lip hypoplasia, and actinic cheek rhytidity. These facial tissues are distinct from the sensitive vocal cord tissues manipulated in the claimed methods. Daniels adds no detail for correcting vocal cord defects and the only mention of vocal cord defects in the document is a passing reference to “Ronberg’s disease and unilateral vocal cord paralysis” (column 4, lines 4-5). As the only discussion of correcting vocal cord defects in the combination of the two documents is this passing reference, the combination of Boss and Daniels fails to teach or suggest the vocal cord corrective surgery methods for claims 1-11 and 19. The combination of Boss and Daniels also fails to teach or suggest methods for growing an extracellular matrix from autologous cells and placing the separated extracellular matrix into tissues adjacent to vocal cord defects, as set forth in claims 16, 17 and 21. Accordingly, the cited combination fails to teach or suggest the claimed methods.

The obviousness rejection may be based upon the rationale that the person of ordinary skill in the art coming across the passing reference to vocal cord defects in Daniels possibly would attempt to correct vocal cord defects by the dermal repair methods of Boss. The Court of Appeals for the Federal Circuit stated that this “obvious to try” approach does not properly lead to a conclusion of obviousness when there is no reasonable likelihood of success (*see, e.g., In re Dow Chemical*, 837 F.2d at 471, 5 USPQ.2d at 1530 (Fed. Cir. 1988)). Here, there was no reasonable expectation for successfully correcting a vocal cord defect based upon the combined teachings of Boss and Daniels. Due to the delicate nature of vocal cord defects, Boss and Daniels fail to provide adequate teachings for correcting such defects and the person of ordinary skill in the art would not have successfully carried out the claimed procedures based upon these cited documents. In contrast, the present specification provides a great level of detail on pages 41 and 42 for correcting vocal cord defects, showing the person of ordinary skill in the art the types of cells and tissues that should be used, the types of needles appropriate for injection, the areas in which the cells and tissues should be injected, and alternative correction methods. Given the complexity of correcting a vocal cord

defect, there was no reasonable expectation that the person of ordinary skill in the art could have successfully corrected such a defect based on the limited teachings of Boss and Daniels.

There also was no motivation for combining Daniels with Boss. Boss discusses methods of using autologous cells for the correction of facial defects. Daniels, however, discusses methods for correcting certain defects by injecting collagen, a protein, and thereby fails to teach or suggest methods of utilizing autologous cells or an extracellular matrix derived from such cells in methods for correcting a vocal cord defect. As the two documents discuss the use of wholly unrelated products for correcting certain defects (*i.e.*, collagen in Daniels and cells in Boss), the person of ordinary skill in the art never would have been motivated to combine the teachings of the two documents.

The Office specifically rejected the subject matter of claim 11 over the combination of Boss and Daniels as Daniels allegedly taught a process of culturing cells in phosphate buffered saline. Daniels, however, described a process of adding a buffered salt solution to collagen to promote collagen polymerization. Daniels does not teach or suggest a method of washing collagen with a buffered salt solution, and therefore, the cited combination fails to teach a method of washing cells with phosphate buffered saline. Thus, the cited combination fails to teach or suggest the subject matter of claim 11.

Accordingly, a *prima facie* showing of obviousness cannot be supported by the combination of Boss and Daniels since this combination fails to teach or suggest the claimed methods, fails to provide a reasonable likelihood for successfully practicing the claimed methods, and there was no motivation to combine the two documents. It is therefore respectfully requested that the Office withdraw the rejections of the claims under 35 U.S.C. § 103 in view of this cited combination.

Rejection of the Claims Over Naughton and Boss

Claims 9-10 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatenable over Naughton and Boss. Claim 9 specifies that the method of claim 1 is performed by placing the cells and the matrix in the subject's tissue by engraftment. Claim 10 specifies that the method of claim 1 is performed by culturing cells *in vitro* using serum from the subject. The rejection was based upon the rationale that Naughton does not disclose methods of culturing autologous cells in serum from

the subject, but Boss provides such a treatment. The rationale for rejecting claim 9 was not specified. The rejection is respectfully traversed.

There was no motivation to combine Boss and Naughton for the subject matter of claim 9, because Naughton teaches away from a method in which cells and the supporting matrix are placed in the tissue by engraftment. Specifically, Naughton explains in paragraphs 68 to 69 that the extracellular matrix is separated from the dead cells and the supporting medium before the extracellular matrix is placed in the tissue by injection. Because Naughton separates the growth matrix from the cells and extracellular matrix before the latter is injected into the defective site, there is a teaching away from placing a combination of the cells and the matrix in the tissue by engraftment. Thus, there was no motivation to combine Naughton and Boss due to this teaching away from the method of claim 9. And because Naughton fails to disclose, teach or suggest methods of retrieving, culturing and returning cells to the same subject, there was no motivation to combine the two documents.

There also was no motivation to combine the cited documents for the subject matter of claim 10 because Naughton discusses methods for destroying cells, separating the destroyed cells and growth support from the extracellular matrix, and then injecting the extracellular matrix into a defective tissue. This process is wholly different than what was discussed in Boss, because instead of destroying cells and separating these from the extracellular matrix, Boss injects cells into a defective tissue. Because the documents teach methods in which wholly different materials are used to correct defects (*i.e.*, an extracellular matrix in Naughton as opposed to an autologous cell in Boss), there was not motivation to combine the teachings of the documents.

Accordingly, a *prima facie* showing of obviousness cannot be supported by the combination of Boss and Naughton as there was no motivation to combine these documents. It is therefore respectfully requested that the rejections of claims 9 and 10 under 35 U.S.C. § 103 be withdrawn.

CONCLUSIONS

It is respectfully requested that the Office withdraw the rejections of the pending claims as Naughton fails to disclose methods for placing viable cells in a position subjacent to a vocal cord defect in the same subject (claims 1-11 and 19). Naughton also fails to disclose a method for collecting an extracellular matrix from cells collected from a subject and placing it in a site in the same subject (claims 16, 17 and 21) or in a site selected from the group consisting of a scar, Reinke's space, a muscle of the vocal cord, and the lamina propria (claim 21). It respectfully is requested that the Office withdraw the obviousness rejections because the combination of Boss and Daniels fails to result in the claimed subject matter, provides no reasonable expectation for successfully correcting a vocal cord defect, and there was no motivation to combine the documents. There also was no motivation to combine Naughton and Boss. It therefore is respectfully submitted that the claims are free of the prior art and it is respectfully requested that the Office issue a Notice of Allowance.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 514072000210. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: October 7, 2003

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